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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/924,647	08/07/2001	Sean Adams	P1219P3	7392
9157	7590 05/14/2003		,	
GENENTECH, INC.			EXAMINER	
I DNA WAY SOUTH SAN FRANCISCO, CA 94080			SAOUD, CH	RISTINE J
	•		ART UNIT	PAPER NUMBER
		•	1647	. 13
	•		DATE MAILED: 05/14/2003	1

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.

Applicant(s)

09/924,647

ADAMS et al.

Office Action Summary

Christine Saoud

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The MAILING DATE of this communication appears on the cover sheet with the correspondence address					
Period for Reply					
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.					
 Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. 					
 If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Amy reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). 					
Status					
1) X Responsive to communication(s) filed on <u>Feb 24, 2</u>	2003				
2a) ☐ This action is FINAL . 2b) ☑ This ac	tion is non-final.				
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.					
Disposition of Claims					
4) 💢 Claim(s) <u>1-95</u>	is/are pending in the application.				
4a) Of the above, claim(s) 22-95	is/are withdrawn from consideration.				
5) Claim(s)	is/are allowed.				
6) 💢 Claim(s) <u>1-21</u>	is/are rejected.				
7) Claim(s)	is/are objected to.				
8) Claims are subject to restriction and/or election requirement.					
Application Papers					
9) 💢 The specification is objected to by the Examiner.					
10) ☐ The drawing(s) filed on is/are a) ☐ accepted or b) ☐ objected to by the Examiner.					
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).					
11)☐ The proposed drawing correction filed on is: a)☐ approved b)☐ disapproved by the Examiner.					
If approved, corrected drawings are required in reply to this Office action.					
12) \square The oath or declaration is objected to by the Examiner.					
Priority under 35 U.S.C. §§ 119 and 120					
13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).					
a) All b) Some* c) None of:					
1. Certified copies of the priority documents have been received.					
2. Certified copies of the priority documents have been received in Application No					
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).					
*See the attached detailed Office action for a list of the certified copies not received.					
14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).					
a) U The translation of the foreign language provisional application has been received.					
15) X Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121. Attachment(s)					
1) X Notice of References Cited (PTO-892)	4) Interview Summary (PTO-413) Paper No(s).				
2) Notice of Draftsperson's Petent Drawing Review (PTO-948)	5) Notice of Informal Patent Application (PTO-152)				
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s).	6) Other:				

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DETAILED ACTION

Election/Restriction

- 1. Applicant's election of Group I, claims 1-21, in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
- 2. Claims 1-21, 32-37 and 39-80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 8.

Priority

An application for patent for an invention disclosed in the manner provided by the

3. 35 U.S.C. §120 states that:

first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application. No application shall be entitled to the benefit of an earlier filed application under this section unless an amendment containing the specific reference to the earlier filed application is submitted at such time during the pendency of the application as required by the Director. The Director may consider the failure to submit such an amendment within that time period as a waiver of any benefit under this section. The Director may establish procedures, including the payment of a surcharge, to accept an unintentionally delayed submission of an amendment under this section.

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The instant application is a continuation-in-part of U.S.S.N 09/767,609, filed January 22, 2001, which is a continuation-in-part of U.S.S.N 09/522,342, filed March 9, 2000, which is a continuation-in-part of U.S.S.N. 09/284,663, filed April 15, 1999. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. §120 from an earlier application which meets the requirements of 35 U.S.C. §112, first paragraph, with respect to the claimed invention. Because prior application, 09/284,663, did not meet the requirements of 35 U.S.C. §112, first paragraph, for the reasons given below, the instant application does not obtain benefit of priority to 09/284,663 under 35 U.S.C. §120.

Application 09/284,663 is directed to a PRO533 polypeptide. The specification of 09/284,663 discloses and claims a protein and nucleic acid of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the PRO533 polypeptide, or the nucleic acid encoding it, of application 09/284,663 can be used for diagnosis, prevention and treatment of cancer and connective tissue disorders as stated at page 1, 4, and 6-7 of the '663 specification. Until some actual and specific significance can be attributed to the protein, identified in the '663 specification as PRO533, or the nucleic acid encoding it, the instant invention is incomplete. The nucleic acid of '663 and the protein encoded thereby are compounds which share some structural similarity to fibroblast growth factor family of proteins based on sequence similarity. The FGF family of proteins share structural similarity but "have now been shown to have diverse activities on cells of mesodermal or neuroectodermal origin with roles including the capacity to promote or inhibit

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differentiated phenotypes during development, mediate angiogenic and neurotrophic effects and modulate cell migration" (see the '663 specification at page 2, lines 26-28). It is not clear which of the biological activities associated with the FGF family would be possessed by the protein of the '663 application, therefore, one would not know how to employ the protein of the '663 application. The '663 specification indicates that PRO533 binds to fibroblast growth factor receptor-4, however, no known biological significance can be attributed to this receptor at this time, especially in view of the fact that "FGFR-4 signaling is proposed to be virtually nonmitogenic" (see the '663 specification at page 32, lines 30-31). The '663 specification indicates that PRO533 "could be used as a reagent to examine and analyze FGFR4 function in complex primary cell systems and animal models", however, this is not a real world utility. In the absence of the biological significance of this protein or the encoding nucleic acid, there is no immediately obvious patentable use for it. To employ a protein of the '663 application in any of the disclosed methods would clearly be using it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the '663 application does not disclose a credible "real world" use for PRO533 or the encoding nucleic acid, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful and does not meet the requirements of 35 U.S.C. §112, first paragraph, failing to adequately teach how to use the invention for those reasons given above with regard to 35 U.S.C. §101.

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Specification

- 4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see at least pages 14 and 16). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.
- 5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed (i.e. not to the polypeptide and methods of use).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 5, 7, 13-15, 17-21 are rejected under 35 U.S.C. 112, first paragraph, as

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 5, 7, 13-15, 17-21 encompass polynucleotides which have at least about 80% sequence identity to SEQ ID NO:1 (or some portion thereof) or to the cDNA contained in an ATCC deposit. However, the instant specification fails to describe a representative number of nucleic acids which are encompassed by these claims, other than the polynucleotide of SEQ ID NO:1. In making a determination of whether the application complies with the written description

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in the prior art.

requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a polynucleotide which has the nucleic acid sequence of SEQ ID NO:1 or is contained within ATCC deposit #209480. The subject matter which is claimed is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are to polynucleotides having 80% identity to SEQ ID NO:1 or to a cDNA contained in an ATCC Deposit. First, the claims are not limited to a molecules with a specific structure. The claims only require the molecules share some degree of structural similarity to the isolated nucleic acid of SEQ ID NO:1. The specification only describes a polynucleotide having the nucleic acid sequence of SEQ ID NO:1 and fails to teach or describe any other molecules which lack the disclosed sequence. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example of each molecule provided in the specification, there is no guidance found

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the

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genus which are encompassed by the instant claims except for the polynucleotide of SEQ ID NO:1. The specification does not provide a complete structure of those polynucleotides which have 80% identity to SEQ ID NO:1 or to the cDNA contained in an ATCC Deposit. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus (those polynucleotides which have 80% identity to SEQ ID NO:1 or to the cDNA contained in an ATCC Deposit) because the specification teaches only the one embodiment for each molecule claimed. Therefore, the claims are directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. Claims 5-8 and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention appears to employ novel vectors and/or microorganisms. Since the microorganism is essential to the claimed invention it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids'

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sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 USC § 112 may be satisfied by a deposit of the plasmid and/or microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the DNA sequences and/or microorganism are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids and/or microorganisms should have been made in accordance with 37 C.F.R. 1.801-1.809.

It is noted that applicants have deposited the organism but there is not indication in the specification as to public availability. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit

requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

during the pendency of this application, access to the invention will be afforded to (a) the Commissioner upon request;

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- (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
- (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
- (d) the deposit will be replaced if it should ever become inviable.
- 9. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 21 is directed to a method of producing a polypeptide. However, the process includes complementary DNA and using such to make a polypeptide. The instant specification fails to teach how the skilled artisan would make a polypeptide utilizing complementary (i.e. non-coding) DNA. Furthermore, the instant specification fails to teach how to make a protein with a nucleic acid molecule that does not encode a protein. Therefore, the instant claim is not enabled for the reasons provided.

- 10. The following is a quotation of the second paragraph of 35 U.S.C. 112:
 - The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
- 11. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 1, 5, 7, and 13 recite "at least about 80%". However, the metes and bounds of "at least about 80%" are unclear as there is no definite lower limit. For example, would 75% be encompassed by "at least about 80%", or is only 78% intended. Without a definite range, the metes and bounds of what are encompassed are indefinite.

Claims 1, 4, 9, 10, and 12 recite "from 1 or about 23 to about 216 of Figure 2". Claims 2 and 10 recite "from about 464 or about 530 to about 1111 of Figure 1". Even though the use of the term "about" in a claim is inherently vague and indefinite, its use is appropriate when employed to limit a value which is composed of infinitely divisible units such as inches, meters, grams and pints where it is impractical to produce an item which has exactly the dimension recited. Even if one could practically produce an item which is exactly 1 inch in length, the length of that item is conditional upon the temperature at which it is measured. However, when defining an invention in terms of indivisible numerical units such as the number of nucleotides in a nucleic acid, the number of amino acids in a polypeptide or the number of legs on a chair or table, the term "about" is unacceptably vague and indefinite since it is practical to employ a term which possesses the required precision. If, for example, it is Applicant's intention that the claims should encompass a polypeptide of no more than 32 amino acids in length then this is exactly what the claim should recite. Whereas one would reasonably interpret the term "about one inch" as encompassing any value from 0.90 inches to 1.10 inches one would not know if the term "from about 23 to about 216" would include or exclude amino acid 22, amino acid 21, or even amino acid 1.

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Claims 1, 9, and 21 are vague and indefinite in reference to the term "FGF-19 polypeptide". Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "FGF-19 polypeptide" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

Furthermore, in the art of FGF molecules, the designation given to the molecules conveys no particular structure and/or function as the initial naming is arbitrary and cannot take into account the discovery of other FGF molecules at a similar time. Therefore, the designation of FGF-19 by one individual may also be referred to as FGF-23 by another individual, and the name fails to convey what is being claimed.

Claims 1, 2, 4, 9, and 10 are vague and indefinite for the recitation of "the sequence" in combination with a range. Again, the recitation of "the" conveys the concept of a single sequence, which is not consistent with the recitation of a range.

Claims 5 and 6 are indefinite for the recitation "encoding the same mature polypeptide encoded by the human protein cDNA". First, it is not clear to what a "human protein cDNA" refers. cDNA molecules are not protein molecules, but they do usually encode proteins. Second, the nature of the protein which is encoded by a cDNA (i.e. mature, precursor, proteolytically processed) is determined by the host cell in which the cDNA is expressed. Therefore, it is not clear what the metes and bounds of "the same mature polypeptide" are meant to be. This fails to

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convey a particular structure and the skilled artisan is not aware of the metes and bounds of "the same mature polypeptide" and therefore, the claims are indefinite.

Claims 11 and 12 require stringent hybridizing conditions, however, the specification fails to adequately describe these conditions. There are several variables which determine the stringency of hybridization, including temperature, salt, probe length, hybridization buffer as well as the wash conditions which are used. The metes and bounds of this limitation cannot be ascertained from the specification as filed, therefore, the claims are indefinite.

Claim 12 recites "comprising at least about 22 nucleotides". However, the metes and bounds of "at least about 22" are unclear as there is no definite lower limit. The combination of "at least" with "about" does not convey any lower limit which is definite, and therefore, the methods and bounds of what is encompassed is indefinite.

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP 2172.01. The omitted steps are: the claim fails to require the test DNA to encode a polypeptide, which is necessary for the production of a polypeptide.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP 2172.01. The omitted steps are: The claim requires a determination of sequence identity for a DNA molecule prior to isolation of the DNA molecule. It would appear that sequence identity determination would require isolation of the DNA, therefore, the order of the steps is either

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backwards, or the claim is missing a step that would provide for the sequence determination of the

test DNA.

All dependent claims are indefinite for depending on the base claims which are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the 12.

basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or

on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishimura 13.

et al. (Biochimica et Biophysica Acta 1444: 148-151, Jan. 18, 1999).

Nishimura et al. teach a polypeptide which is 100% identical to that of SEQ ID NO:2 (see

Figure 1) as well as a nucleic acid which is 100% identical to that of the claimed SEQ ID NO:1.

Therefore, the claims are anticipated by Nishimura et al.

Applicant should note that in the absence of hybridizing conditions, claim 12 encompasses

the majority of nucleic acids in existence. Art will not be applied to the extent of the breadth of

the claim, but Applicant should clearly note that most nucleic acids will hybridize and with a lack

of wash conditions, most nucleic acids will remain stuck to the sample DNA molecule. Therefore,

the claim encompasses DNA molecules with relatively few nucleotides in common with SEQ ID

NO:1.

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Claim Rejections - 35 USC § 103

- 14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 15. Claims 1, 14, 15, and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishimura et al. (Biochimica et Biophysica Acta 1444: 148-151, Jan. 18, 1999) in view of U.S. Pat No. 6,013,477 (Greene et al.).

The instant claims encompass vectors, host cells (CHO, E. coli and yeast), operably linked molecules to control sequences for the host cells, as well as recombinant methods of producing the encoded protein. Nishimura et al. do not teach vectors, host cells, or recombinant methods of producing the encoded protein. Greene et al. teach recombinant methods of producing an FGF protein, including vectors (see column 8, especially line 65 to column 9, line 6), control sequences (see column 8, and especially column 9, lines 7-15), host cells (see column 8), as well as recombinant methods of protein production (see column 10). Green et al. do not teach vectors, host cells and recombinant methods of production of the claimed nucleic acid. However, the instant specification indicates at pages 47-51 that preparation of vectors, expression of the encoded protein, host cell transformation and isolation of the encoded polypeptide could be

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performed using methods which are known in the art because such methods are old and well-known in the art.

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It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to place the nucleic acid molecule of Nishimura et al. into a vector with the proper control sequences in order to transform a host cell and produce the encoded polypeptide by the methods and with the reagents of Greene et al. for the purposes of making the encoded protein described by Nishimura et al. One would be motivated to produce the polypeptide described by Nishimura et al. because it is described as a new member of the FGF family which is expressed in the fetal brain, and recombinant production would produce larger quantities of the protein for further research. One would have a reasonable expectation of producing the vectors, host cells, and the protein because such methods were recognized to be old and well-known in the art, especially in relation to FGF proteins as evidenced by the instant specification and by the art of Greene et al. Therefore, the invention as claimed would have been *prima facie* obvious to one of ordinary skill in the art at the time the application was filed, absent evidence to the contrary.

Conclusion

16. No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The Examiner can normally be reached on Monday to Thursday from 8AM to 2PM. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §§ 1.6(d) and 1.8). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternate number. Official papers filed After Final rejection filed by fax should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CHRISTINE J. SAOUD PRIMARY EXAMINER

Thustine J. Saoua